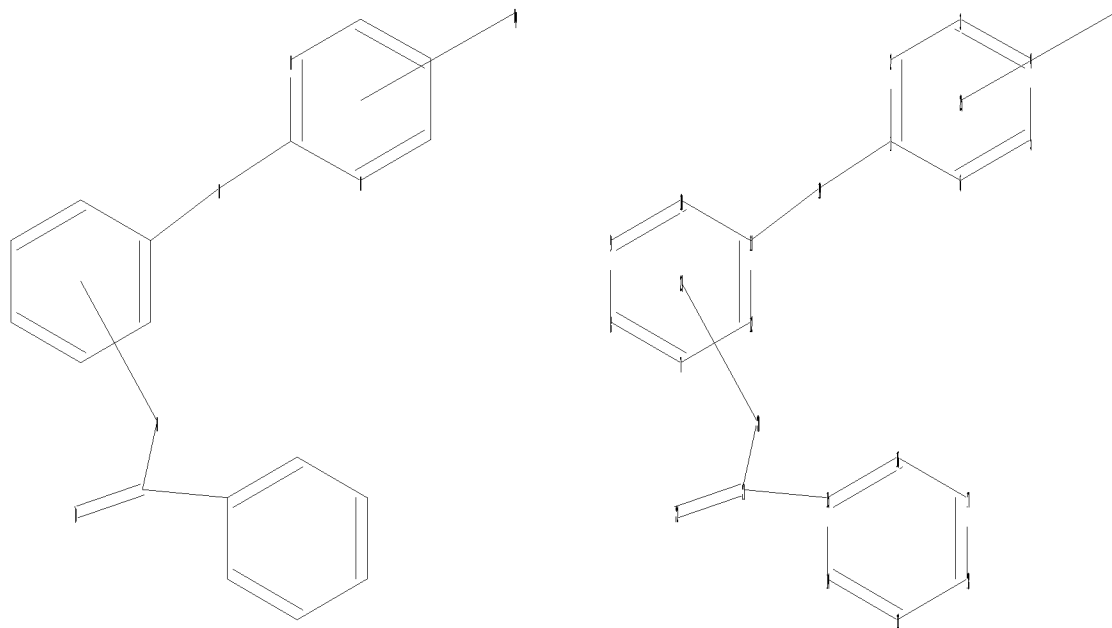


=&gt;

Uploading C:\Program Files\Stnexp\Queries\10502291.str



```

chain nodes :
19 20 21 22 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-19 11-19 15-21 20-21 21-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
exact/norm bonds :
1-19 11-19 20-21 21-22
exact bonds :
15-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 :

```

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom

```

Generic attributes :

24:

```

Saturation           : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System   : Monocyclic

```

10/502,291

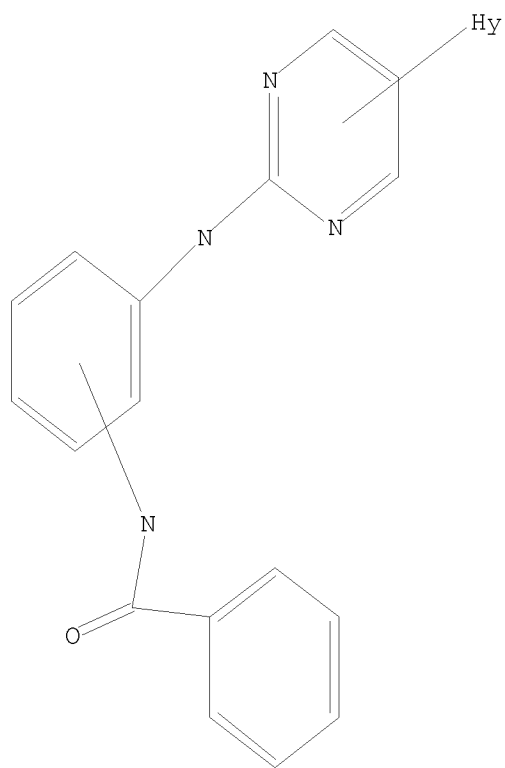
Element Count :  
Node 24: Limited  
C,C5  
N,N1  
O,O0  
S,S0

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 11:54:00 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2723 TO ITERATE

73.4% PROCESSED 2000 ITERATIONS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

9 ANSWERS

10/502,291

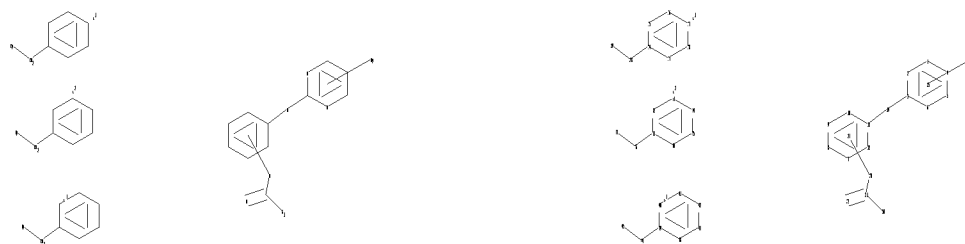
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 51330 TO 57590  
PROJECTED ANSWERS: 35 TO 455

L2 9 SEA SSS SAM L1

=> =>

Uploading C:\Program Files\Stnexp\Queries\10502291 (a).str



chain nodes :  
19 20 21 22 24 28 29 36 37 44 45 50  
ring nodes :  
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 30 31 32 33 34  
35 38 39 40 41 42 43  
chain bonds :  
1-19 11-19 14-28 20-21 21-22 21-50 28-29 31-36 36-37 39-44 44-45  
ring bonds :  
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
14-15 15-16 16-17 17-18 30-31 30-35 31-32 32-33 33-34 34-35 38-39 38-43  
39-40 40-41 41-42 42-43  
exact/norm bonds :  
1-19 11-19 20-21 21-22 21-50 28-29 36-37 44-45  
exact bonds :  
14-28 31-36 39-44  
normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
 14-15 15-16 16-17 17-18 30-31 30-35 31-32 32-33 33-34 34-35 38-39 38-43  
 39-40 40-41 41-42 42-43  
 isolated ring systems :  
 containing 1 : 7 : 13 : 30 : 38 :

G1:[\*1],[\*2],[\*3]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS  
 20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom 28:CLASS 29:Atom 30:Atom  
 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom 36:CLASS 37:Atom 38:Atom 39:Atom  
 40:Atom 41:Atom 42:Atom 43:Atom 44:CLASS 45:Atom 50:CLASS

Generic attributes :

24:

Saturation : Unsaturated  
 Number of Carbon Atoms : less than 7  
 Number of Hetero Atoms : Exactly 1  
 Type of Ring System : Monocyclic

Element Count :

Node 24: Limited

C,C5  
 N,N1  
 O,O0  
 S,S0

L3 STRUCTURE UPLOADED

=> d 13

L3 HAS NO ANSWERS

L3 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s 13 sss sam

SAMPLE SEARCH INITIATED 12:00:04 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 265 TO ITERATE

100.0% PROCESSED 265 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 4324 TO 6276

PROJECTED ANSWERS: 8 TO 329

10/502,291

L4 8 SEA SSS SAM L3

=> => s l3 sss ful

FULL SEARCH INITIATED 12:01:49 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 5275 TO ITERATE

100.0% PROCESSED 5275 ITERATIONS

198 ANSWERS

SEARCH TIME: 00.00.01

L5 198 SEA SSS FUL L3

=> => s l5

L6 3032 L5

=> => ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=> screen 1719

L7 SCREEN CREATED

=>

Uploading C:\Program Files\Stnexp\Queries\10502291 (b).str



chain nodes :

19 20 21 22 24 28 29 36 37 44 45 50

```

ring nodes :
1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17 18 30 31 32 33 34
35 38 39 40 41 42 43
chain bonds :
1-19 11-19 14-28 20-21 21-22 21-50 28-29 31-36 36-37 39-44 44-45
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18 30-31 30-35 31-32 32-33 33-34 34-35 38-39 38-43
39-40 40-41 41-42 42-43
exact/norm bonds :
1-19 11-19 20-21 21-22 21-50 28-29 36-37 44-45
exact bonds :
14-28 31-36 39-44
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18 30-31 30-35 31-32 32-33 33-34 34-35 38-39 38-43
39-40 40-41 41-42 42-43
isolated ring systems :
containing 1 : 7 : 13 : 30 : 38 :

```

```
G1:[*1],[*2],[*3]
```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom 28:CLASS 29:Atom 30:Atom
31:Atom 32:Atom 33:Atom 34:Atom 35:Atom 36:CLASS 37:Atom 38:Atom 39:Atom
40:Atom 41:Atom 42:Atom 43:Atom 44:CLASS 45:Atom 50:CLASS
Generic attributes :
24:
Saturation           : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System   : Monocyclic

```

```

Element Count :
Node 24: Limited
  C,C5
  N,N1
  O,O0
  S,S0

```

```
L8      STRUCTURE UPLOADED
```

```
=> que L8 AND L7
```

```
L9      QUE L8 AND L7
```

```
=> d 19
```

```
L9 HAS NO ANSWERS
```

```
L7      SCR 1719
```

L8 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

L9 QUE L8 AND L7

=> s 19 sss sam

SAMPLE SEARCH INITIATED 12:07:26 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L8 AND L7

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=> screen 2005 AND 1842

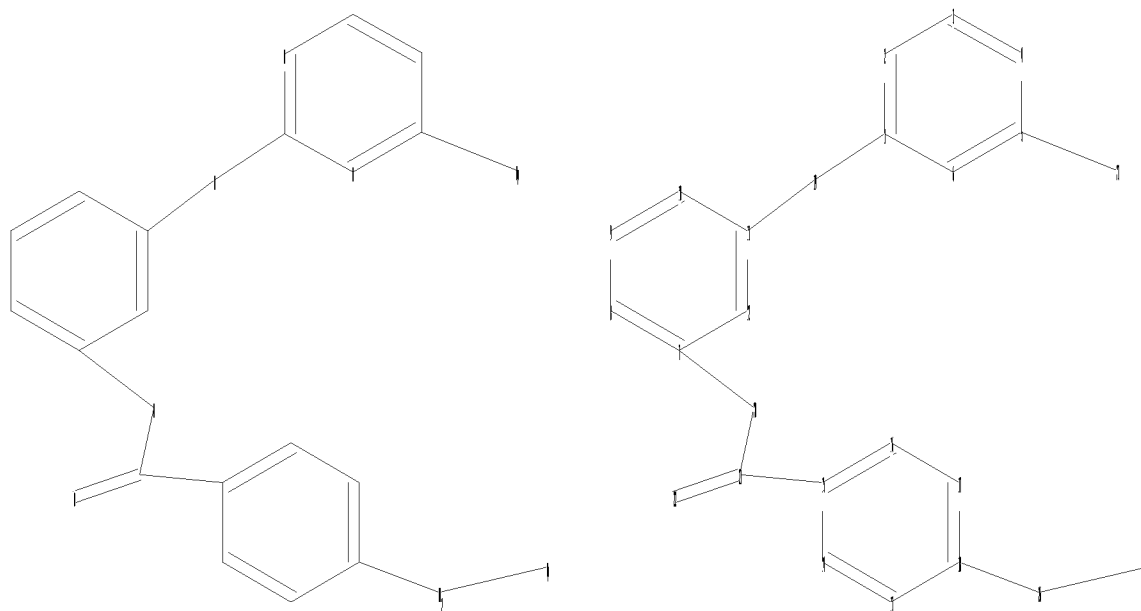
L11 SCREEN CREATED

=> screen 2016 OR 2026 OR 2039 OR 2045 OR 2047

L12 SCREEN CREATED

=>

Uploading C:\Program Files\Stnexp\Queries\10502291 (c).str



```

chain nodes :
19 20 21 22 23 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-19 5-23 7-20 11-19 15-21 18-26 20-21 21-22 26-27
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
exact/norm bonds :
1-19 5-23 7-20 11-19 20-21 21-22 26-27
exact bonds :
15-21 18-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 :

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 26:CLASS 27:CLASS
Generic attributes :
23:
Saturation           : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System   : Monocyclic
27:
Type of Ring System   : Monocyclic

```



Element Count :  
Node 23: Limited  
C,C5  
N,N1  
O,O0  
S,S0

L13 STRUCTURE UPLOADED

=> que L13 AND L11 NOT L12

L14 QUE L13 AND L11 NOT L12

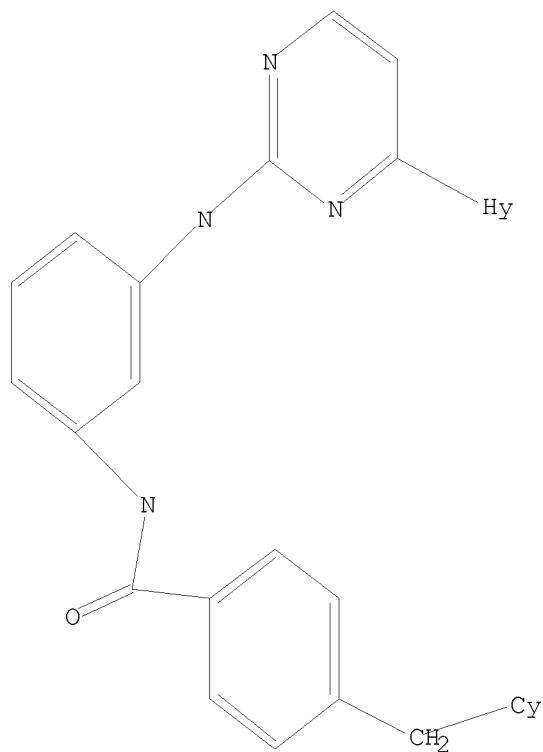
=> d l14

L14 HAS NO ANSWERS

L11 SCR 2005 AND 1842

L12 SCR 2016 OR 2026 OR 2039 OR 2045 OR 2047

L13 STR



Structure attributes must be viewed using STN Express query preparation.  
L14 QUE L13 AND L11 NOT L12

10/502,291

=> s 114 sss sam

SAMPLE SEARCH INITIATED 12:12:33 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 19 TO ITERATE

100.0% PROCESSED 19 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 119 TO 641

PROJECTED ANSWERS: 5 TO 234

L15 5 SEA SSS SAM L13 AND L11 NOT L12

=> => ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=> screen 2005 AND 1842

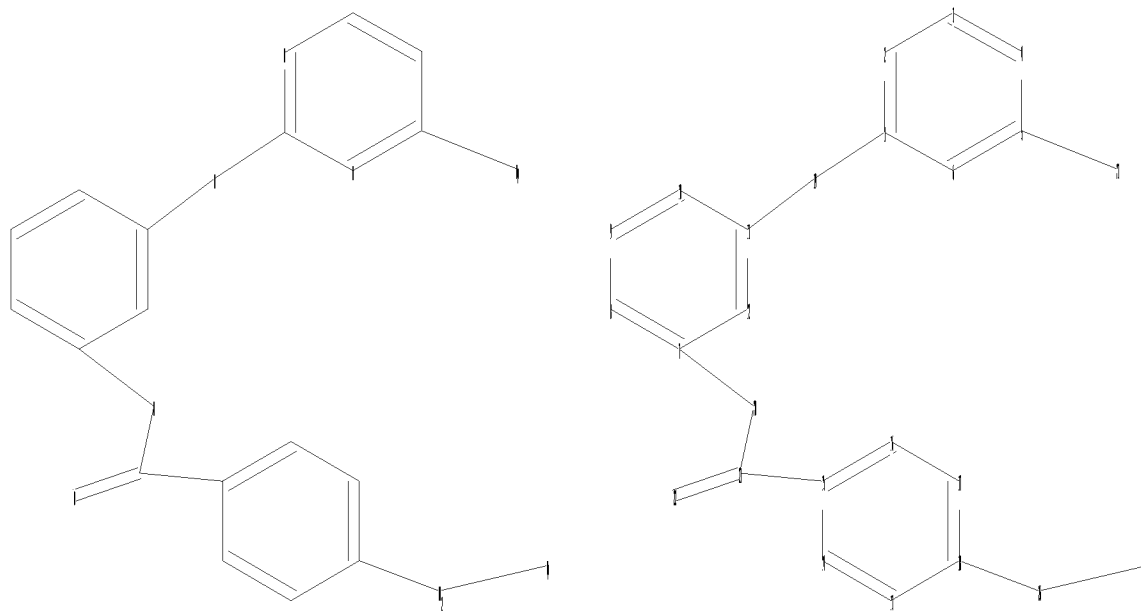
L16 SCREEN CREATED

=> screen 2016 OR 2026 OR 2039 OR 2045 OR 2047 OR 2127

L17 SCREEN CREATED

=>

Uploading C:\Program Files\Stnexp\Queries\10502291 (d).str



chain nodes :

19 20 21 22 23 26 27

ring nodes :

10/502,291

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18  
chain bonds :  
1-19 5-23 7-20 11-19 15-21 18-26 20-21 21-22 26-27  
ring bonds :  
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
14-15 15-16 16-17 17-18  
exact/norm bonds :  
1-19 5-23 7-20 11-19 20-21 21-22 26-27  
exact bonds :  
15-21 18-26  
normalized bonds :  
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
14-15 15-16 16-17 17-18  
isolated ring systems :  
containing 1 : 7 : 13 :

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:Atom 26:CLASS 27:CLASS  
Generic attributes :  
23:  
Saturation : Unsaturated  
Number of Carbon Atoms : less than 7  
Number of Hetero Atoms : Exactly 1  
Type of Ring System : Monocyclic  
27:  
Type of Ring System : Monocyclic  
  
Element Count :  
Node 23: Limited  
C,C5  
N,N1  
O,O0  
S,S0

L18 STRUCTURE UPLOADED

=> que L18 AND L16 NOT L17

L19 QUE L18 AND L16 NOT L17

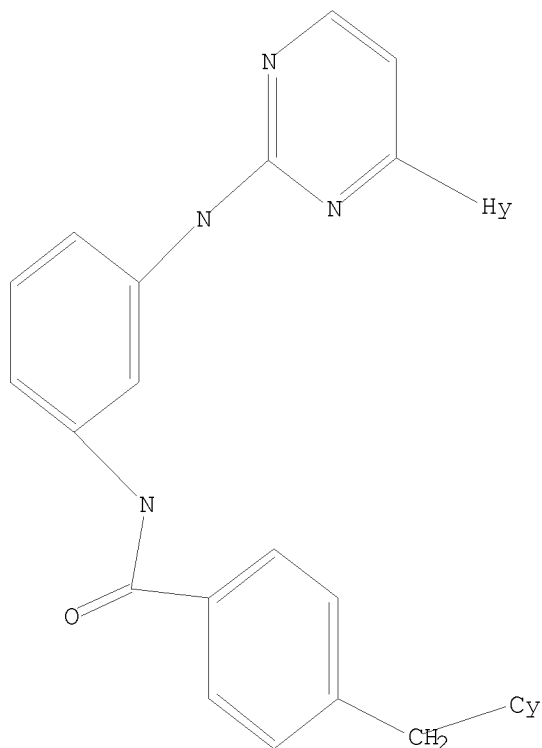
=> d 119

L19 HAS NO ANSWERS

L16 SCR 2005 AND 1842

L17 SCR 2016 OR 2026 OR 2039 OR 2045 OR 2047 OR 2127

L18 STR



Structure attributes must be viewed using STN Express query preparation.  
 L19 QUE L18 AND L16 NOT L17

=> s l19 sss sam  
 SAMPLE SEARCH INITIATED 12:15:07 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 1 ANSWERS  
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*  
 PROJECTED ITERATIONS: 22 TO 418  
 PROJECTED ANSWERS: 1 TO 80

L20 1 SEA SSS SAM L18 AND L16 NOT L17

=> => s l19 sss ful  
 FULL SEARCH INITIATED 12:15:44 FILE 'REGISTRY'  
 FULL SCREEN SEARCH COMPLETED - 127 TO ITERATE

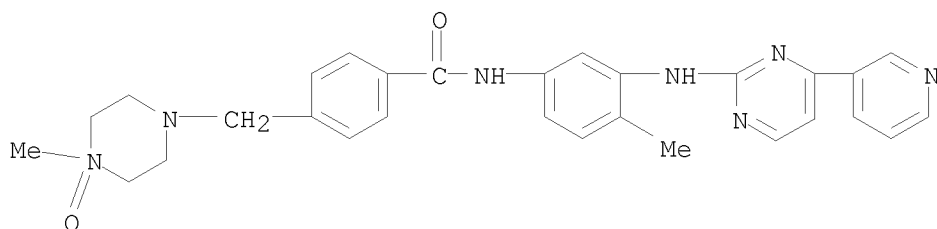
100.0% PROCESSED 127 ITERATIONS 26 ANSWERS  
 SEARCH TIME: 00.00.01

L21 26 SEA SSS FUL L18 AND L16 NOT L17

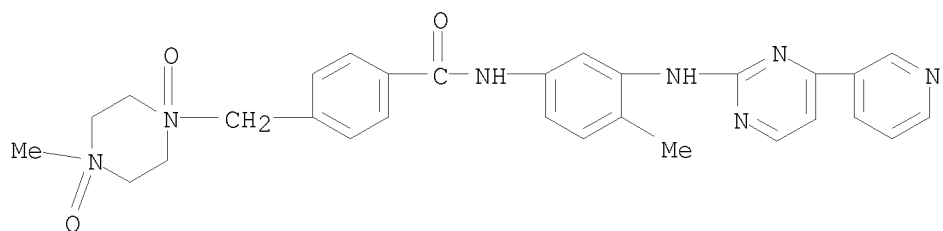
10/502,291

```
=> => s 121
L22      14 L21
=> d 122 1-14 bib,ab,hitstr
```

L22 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2007:345353 CAPLUS  
 DN 147:39589  
 TI Identification of imatinib mesylate degradation products obtained under stress conditions  
 AU Szczepek, W. J.; Kosmacinska, B.; Bielejewska, A.; Luniewski, W.; Skarzynski, M.; Rozmarynowska, D.  
 CS Pharmaceutical Research Institute, Warsaw, 01-793, Pol.  
 SO Journal of Pharmaceutical and Biomedical Analysis (2007), 43(5), 1682-1691  
 CODEN: JPBADA; ISSN: 0731-7085  
 PB Elsevier B.V. not prior  
 DT Journal  
 LA English  
 AB In this paper, the decomposition of imatinib mesylate (ImM) under hydrolytic (neutral, acidic, alkaline), oxidative and photolytic conditions was studied. The imatinib mesylate is practically photostable and stable under neutral conditions. The main degradation products under acidic and alkaline conditions are compds.: 4-methyl-N 3-(4-pyridin-3-yl-pyrimidin-2-yl)-benzene-1,3-diamine and 4-(4-methyl-piperazin-1-ylmethyl)-benzoic acid. The main degradation products under oxidation conditions, i.e. 4-[(4-methyl-4-oxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide, 4-[(4-methyl-1-oxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide and 4-[(4-methyl-1,4-dioxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide, were isolated from the reaction mixts. and identified by the HPLC, <sup>1</sup>H NMR and MS techniques. During stress study the suitability of the proposed HPLC method to control purity of the samples was verified.  
 IT 571186-91-9 571186-93-1 938082-57-6  
 RL: OCU (Occurrence, unclassified); PEP (Physical, engineering or chemical process); OCCU (Occurrence); PROC (Process)  
 (imatinib mesylate degradation products identification obtained under stress conditions)  
 RN 571186-91-9 CAPLUS  
 CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

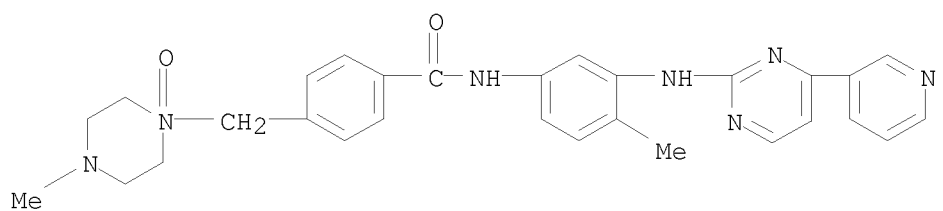


RN 571186-93-1 CAPLUS  
 CN Benzamide, 4-[(4-methyl-1,4-dioxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 938082-57-6 CAPLUS

CN Benzamide, 4-[(4-methyl-1-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

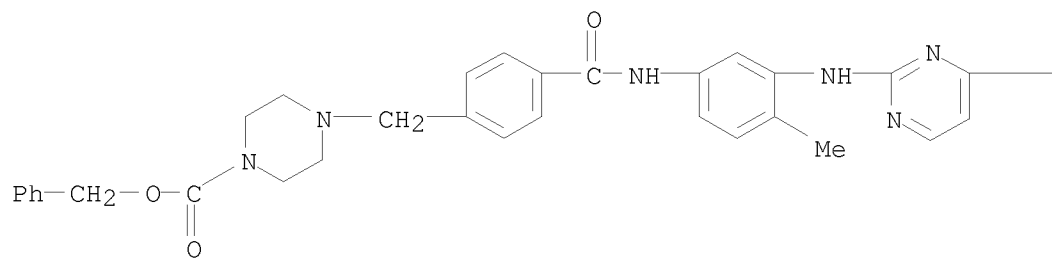


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

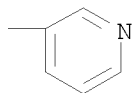
L22 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2007:187945 CAPLUS  
 DN 146:437129  
 TI Synthesis and positron emission tomography studies of carbon-11-labeled imatinib (Gleevec)  
 AU Kil, Kun-Eek; Ding, Yu-Shin; Lin, Kuo-Shyan; Alexoff, David; Kim, Sung Won; Shea, Colleen; Xu, Youwen; Muench, Lisa; Fowler, Joanna S.  
 CS Medical Department, Brookhaven National Laboratory, Upton, NY, 11973, USA  
 SO Nuclear Medicine and Biology (2007), 34(2), 153-163  
 CODEN: NMBIEO; ISSN: 0969-8051  
 PB Elsevier Inc. not prior  
 DT Journal  
 LA English  
 AB Introduction: Imatinib mesylate (Gleevec) is a well known drug for treating chronic myeloid leukemia and gastrointestinal stromal tumors. Its active ingredient, imatinib (4-[[4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridyl)-2-pyrimidinyl]amino]phenyl]benzamide), blocks the activity of several tyrosine kinases. Here we labeled imatinib with carbon-11 as a tool for determining the drug distribution and pharmacokinetics of imatinib, and we carried out positron emission tomog. (PET) studies in baboons. Methods: [N-11C-methyl]imatinib was synthesized from [11C]methyl iodide and norimatinib was synthesized by the demethylation of imatinib (isolated from Gleevec tablets) according to a patent procedure [Collins JM, Klecker RW Jr, Anderson LW, Imaging of drug accumulation as a guide to antitumor therapy. US Patene 20030198594A1, 2003.]. Norimatinib was also synthesized from the corresponding amine and acid. PET studies were carried out in three baboons to measure pharmacokinetics in the brain and peripheral organs and to determine the effect of a therapeutic dose of imatinib. Log D and plasma protein binding were also measured. Results: [N-11C-methyl]imatinib uptake in the brain is negligible (consistent with P-glycoprotein-mediated efflux); it peaks and clears rapidly from the heart, lungs and spleen. Peak uptake and clearance occur more slowly in the liver and kidneys, followed by accumulation in the gallbladder and urinary bladder. Pretreatment with imatinib did not change uptake in the heart, lungs, kidneys and spleen, and increased uptake in the liver and gallbladder. Conclusions: [N-11C-methyl]imatinib has potential for assessing the regional distribution and kinetics of imatinib in the human body to determine whether the drug targets tumors and to identify other organs to which the drug or its labeled metabolites distribute. Paired with tracers such as 2'-deoxy-2'-[18F]fluoro-D-glucose (18FDG) and 3'-deoxy-3'-[18F]fluorothymidine (18FLT), [N-11C-methyl]imatinib may be a useful radiotracer for planning chemotherapy, for monitoring response to treatment and for assessing the role of drug pharmacokinetics in drug resistance.  
 IT 934683-38-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and PET studies of 11C-labeled imatinib for determining imatinib pharmacokinetics)  
 RN 934683-38-2 CAPLUS  
 CN 1-Piperazinecarboxylic acid, 4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]-, phenylmethyl ester (CA INDEX NAME)



PAGE 1-A



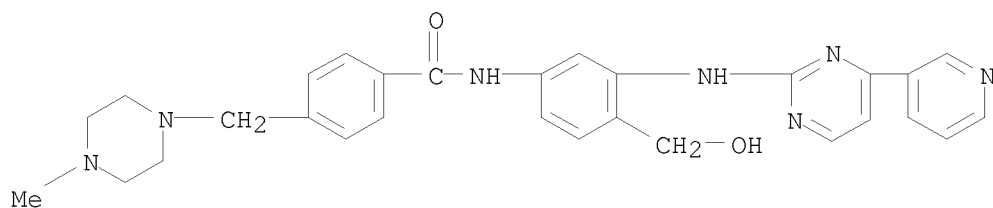
PAGE 1-B



RE.CNT 54

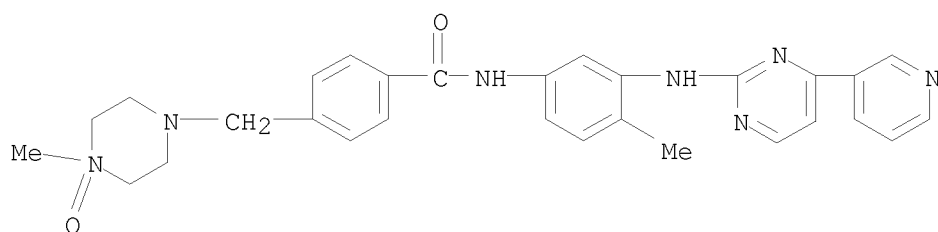
THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2005:1068885 CAPLUS  
DN 143:338914  
TI Metabolism and disposition of imatinib mesylate in healthy volunteers  
AU Gschwind, Hans-Peter; Pfaar, Ulrike; Waldmeier, Felix; Zollinger, Markus;  
Sayer, Claudia; Zbinden, Peter; Hayes, Michael; Pokorny, Rolf; Seiberling,  
Michael; Ben-Am, Monique; Peng, Bin; Gross, Gerhard  
CS Exploratory Development/Drug Metabolism & Pharmacokinetics, Novartis  
Pharma AG, Basel, Switz.  
SO Drug Metabolism and Disposition (2005), 33(10), 1503-1512 not prior  
CODEN: DMDSAI; ISSN: 0090-9556  
PB American Society for Pharmacology and Experimental Therapeutics  
DT Journal  
LA English  
AB Imatinib mesylate (GLEEVEC, GLIVEC, formerly STI571) has demonstrated  
unprecedented efficacy as first-line therapy for treatment for all phases  
of chronic myelogenous leukemia and metastatic and unresectable malignant  
gastrointestinal stromal tumors. Disposition and biotransformation of  
imatinib were studied in four male healthy volunteers after a single oral  
dose of 239 mg of <sup>14</sup>C-labeled imatinib mesylate. Biol. fluids were  
analyzed for total radioactivity, imatinib, and its main metabolite  
CGP74588. Metabolite patterns were determined by radio-high-performance liquid  
chromatog. with off-line microplate solid scintillation counting and  
characterized by liquid chromatog.-mass spectrometry. Imatinib treatment  
was well tolerated without serious adverse events. Absorption was rapid  
(t<sub>max</sub> 1-2 h) and complete with imatinib as the major radioactive compound in  
plasma. Maximum plasma concns. were 0.921±0.095 µg/mL (mean ±  
S.D., n = 4) for imatinib and 0.115±0.026 µg/mL for the pharmacol.  
active N-desmethyl metabolite (CGP74588). Mean plasma terminal  
elimination half-lives were 13.5±0.9 h for imatinib, 20.6±1.7 h for  
CGP74588, and 57.3±12.5 h for <sup>14</sup>C radioactivity. Imatinib was  
predominantly cleared through oxidative metabolism. Approx. 65 and 9% of total  
systemic exposure [AUC<sub>0-24 h</sub> (area under the concentration time curve) of  
radioactivity] corresponded to imatinib and CGP74588, resp. The remaining  
proportion corresponded mainly to oxidized derivs. of imatinib and  
CGP74588. Imatinib and its metabolites were excreted predominantly via  
the biliary-fecal route. Excretion of radioactivity was slow with a mean  
radiocarbon recovery of 80% within 7 days (67% in feces, 13% in urine).  
Approx. 28 and 13% of the dose in the excreta corresponded to imatinib and  
CGP74588, resp.  
IT 571186-90-8, AFN 911 571186-91-9, CGP 71422  
571186-92-0, CGP 72383 571186-94-2, APG 049  
571186-95-3, APG 050 571186-95-3D, glucuronides  
865487-49-6 865487-49-6D, glucuronides  
865487-52-1 865487-52-1D, glucuronides  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(metabolism and disposition of imatinib mesylate in healthy volunteers)  
RN 571186-90-8 CAPLUS  
CN Benzamide, N-[4-(hydroxymethyl)-3-[[4-(3-pyridinyl)-2-  
pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX  
NAME)



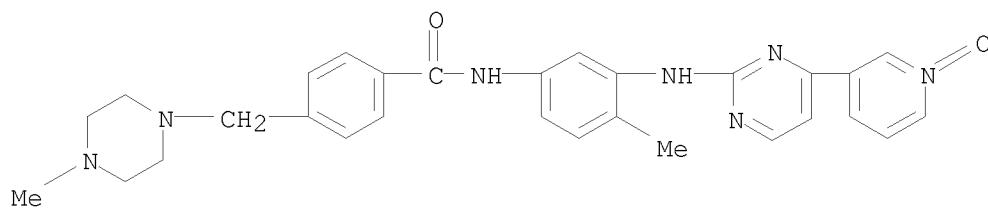
RN 571186-91-9 CAPLUS

CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



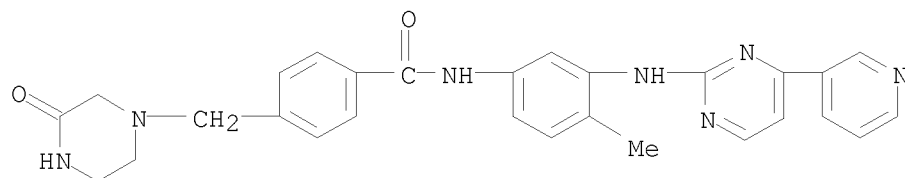
RN 571186-92-0 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(1-oxido-3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



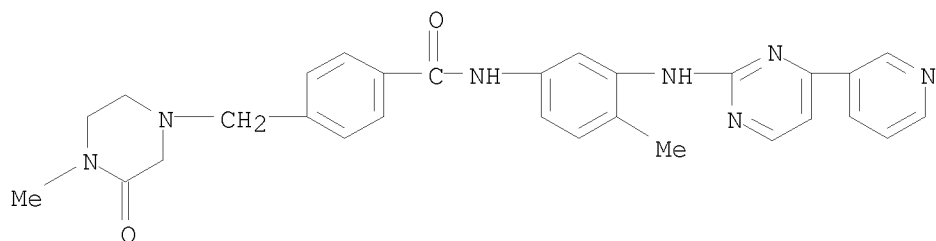
RN 571186-94-2 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(3-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



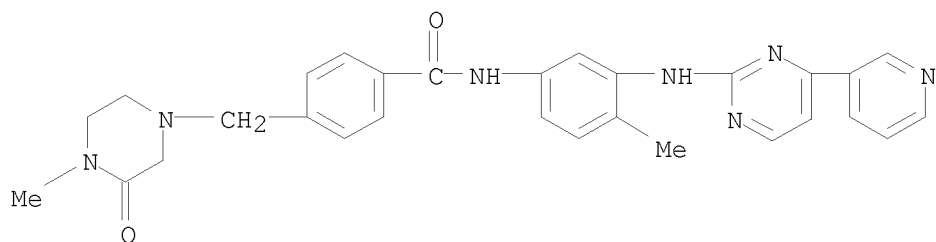
RN 571186-95-3 CAPLUS

CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



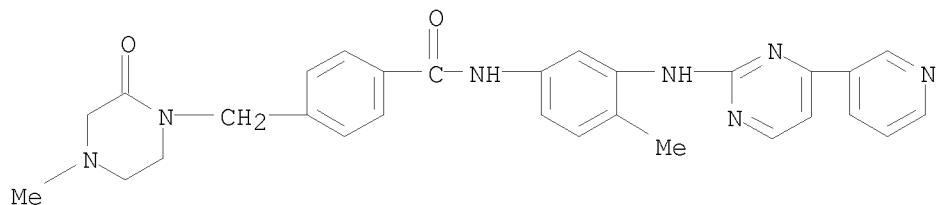
RN 571186-95-3 CAPLUS

CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



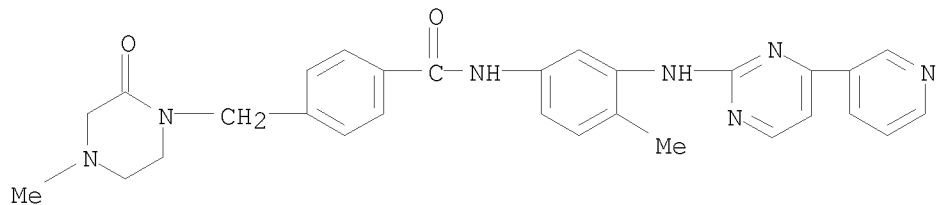
RN 865487-49-6 CAPLUS

CN Benzamide, 4-[(4-methyl-2-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



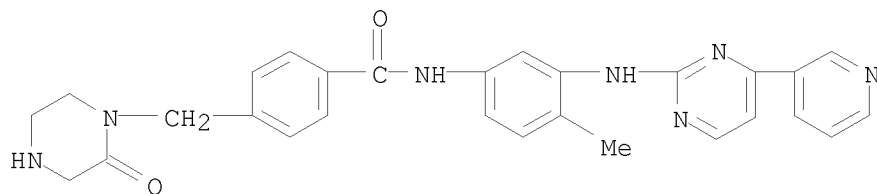
RN 865487-49-6 CAPLUS

CN Benzamide, 4-[(4-methyl-2-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



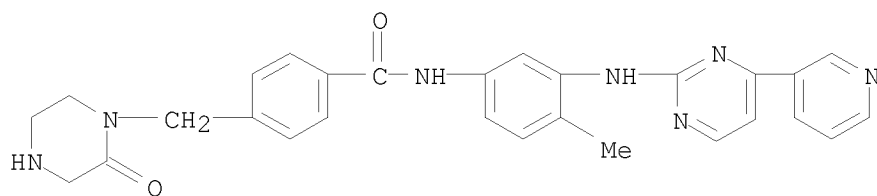
RN 865487-52-1 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-  
[(2-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



RN 865487-52-1 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-  
[(2-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:614536 CAPLUS

DN 143:115392

TI Preparation of conjugated small molecules for diagnostic and therapeutic use

IN Grotzfeld, Robert M.; Milanov, Zdravko V.; Patel, Hitesh K.; Lai, Andiliy G.; Mehta, Shamal A.; Lockhart, David J.

PA Ambit Biosciences Corp., USA

SO U.S. Pat. Appl. Publ., 63 pp.

CODEN: USXXCO

DT Patent

not prior

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005153371	A1	20050714	US 2005-31638	20050107
	AU 2005204428	A1	20050728	AU 2005-204428	20050107
	CA 2551495	A1	20050728	CA 2005-2551495	20050107
	WO 2005067644	A2	20050728	WO 2005-US456	20050107
	WO 2005067644	A3	20051013		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1711825	A2	20061018	EP 2005-705221	20050107
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R: AT, BE, CH, DE, DK, ES, FR, GE, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

JP 2007521338	T	20070802	JP 2006-549423	20050107
PRAI US 2004-535173P	P	20040107		
US 2004-557941P	P	20040330		
WO 2005-US456	W	20050107		

AB Provided herein are linker compds. and conjugates that include the linker compds. In one embodiment, the linker compds. comprise 2 or 3 residues of 6-aminohexanoic acid and optionally 7-10 residues of polyethyleneglycol (PEG). The linker compds. are useful in forming conjugates with one or more components useful in biopharmaceutical or bioanal. applications. In particular, the biopharmaceutically useful compds. are kinase inhibitors. The conjugates described herein have utility in a variety of diagnostic, separation, and therapeutic applications. Thus, I was prepared from SB 202190, PEG-azide and the biotin-linker compound

IT 857892-08-1P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

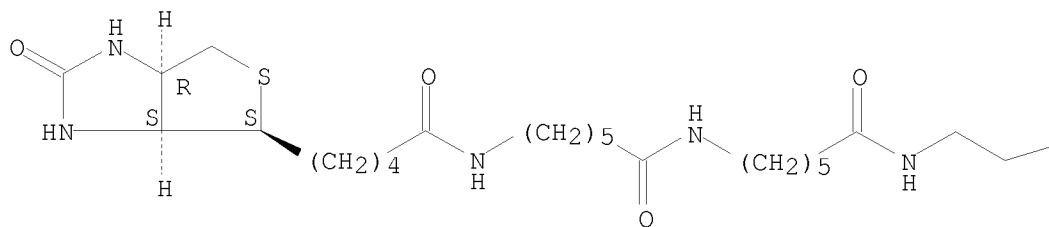
(preparation of conjugated biotins for diagnostic and therapeutic use)

RN 857892-08-1 CAPLUS

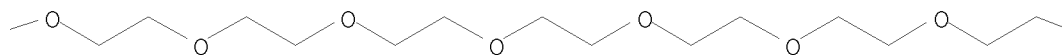
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, hexahydro-N-[37-[4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]-1-piperazinyl]-6,13-dioxo-17,20,23,26,29,32,35-hepta-7,14-diazaheptatriacont-1-yl]-2-oxo-, (3aS,4S,6aR)- (CA INDEX NAME)

Absolute stereochemistry.

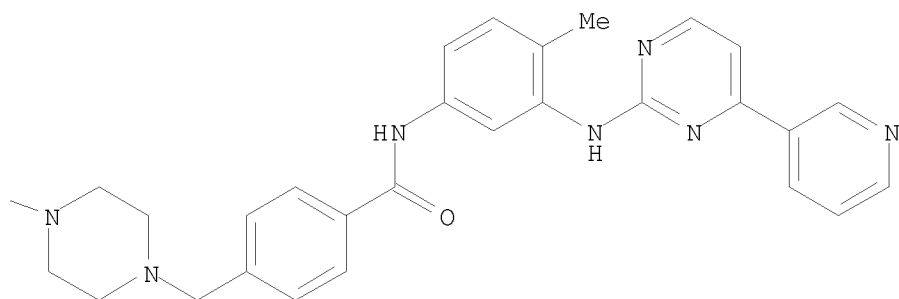
PAGE 1-A



PAGE 1-B



PAGE 1-C



L22 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2005:612254 CAPLUS  
 DN 143:133396  
 TI Preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase inhibitors  
 IN Asaki, Tetsuo; Sugiyama, Yukiteru; Segawa, Jun  
 PA Nippon Shinyaku Co., Ltd., Japan  
 SO PCT Int. Appl., 168 pp.  
 CODEN: PIXXD2 not prior  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005063709	A1	20050714	WO 2004-JP19553	20041227
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004309248	A1	20050714	AU 2004-309248	20041227
	CA 2551529	A1	20050714	CA 2004-2551529	20041227
	EP 1702917	A1	20060920	EP 2004-807908	20041227
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	CN 1898208	A	20070117	CN 2004-80039048	20041227
	BR 2004018074	A	20070417	BR 2004-18074	20041227
	MX 2006PA07237	A	20060818	MX 2006-PA7237	20060622
	IN 2006CN02337	A	20070705	IN 2006-CN2337	20060626
PRAI	JP 2003-431398	A	20031225		
	WO 2004-JP19553	W	20041227		

OS MARPAT 143:133396

AB The title compds. I (R1 represents CH2R11 (R11 represents a nitrogenous saturated heterocyclic group), etc.; R2 represents alkyl, halogeno, haloalkyl, etc.; R3 represents hydrogen, halogeno, alkoxy; Het1 represents Q1, etc.; and Het2 represents pyrimidinyl, etc.) are prepared Thus 3-difluoromethyl-4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl]benzamide was prepared from 4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]aniline and 3-difluoromethyl-4-(4-methylpiperazin-1-ylmethyl)benzoyl chloride HCl salt. In an assay (for cell proliferation inhibiting activity) using K562 cells, compds. of this invention showed IC50 values of < 0.00001  $\mu$ M to 0.001  $\mu$ M. Formulations are given.

IT 859211-72-6P

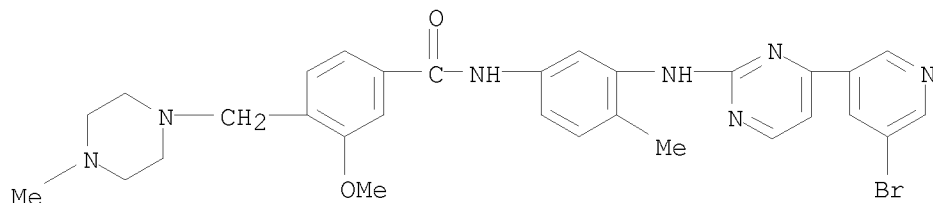
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase inhibitors)

RN 859211-72-6 CAPLUS



CN Benzamide, N-[3-[[4-(5-bromo-3-pyridinyl)-2-pyrimidinyl]amino]-4-methylphenyl]-3-methoxy-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



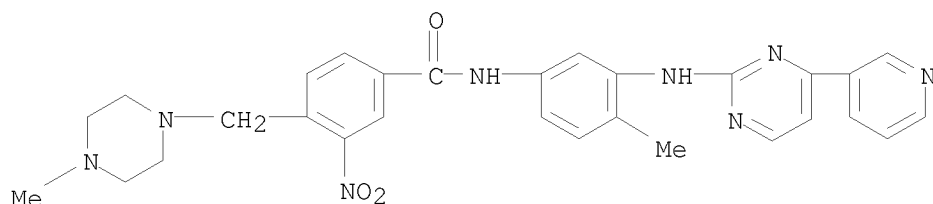
IT 641615-04-5P 641615-05-6P 641615-07-8P  
641615-08-9P 641615-15-8P 641615-21-6P  
859213-57-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase inhibitors)

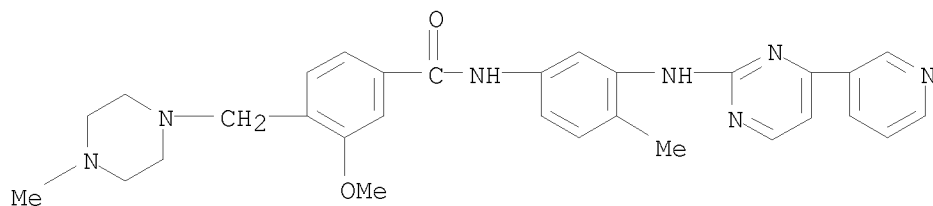
RN 641615-04-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-3-nitro- (CA INDEX NAME)



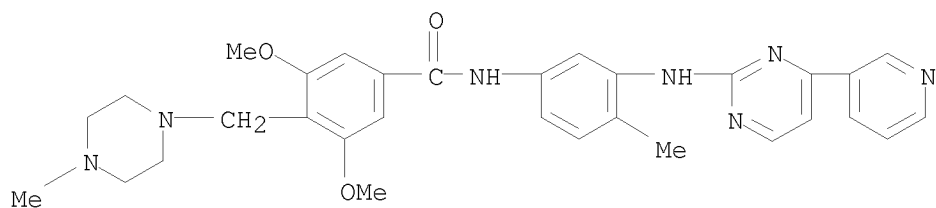
RN 641615-05-6 CAPLUS

CN Benzamide, 3-methoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



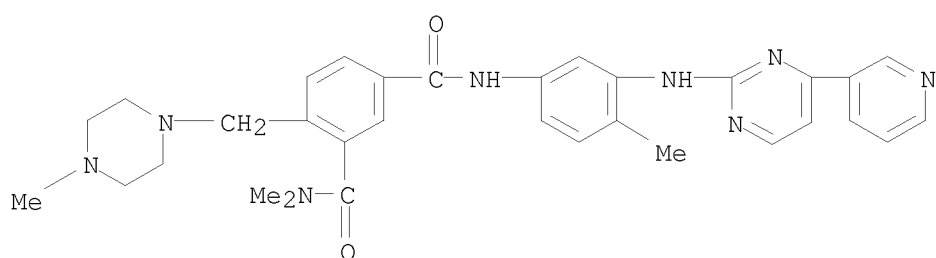
RN 641615-07-8 CAPLUS

CN Benzamide, 3,5-dimethoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



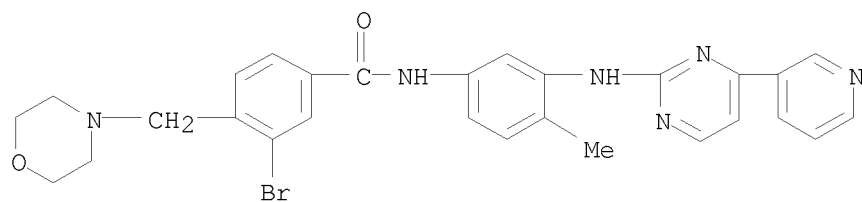
RN 641615-08-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N3,N3-dimethyl-4-[(4-methyl-1-piperazinyl)methyl]-N1-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



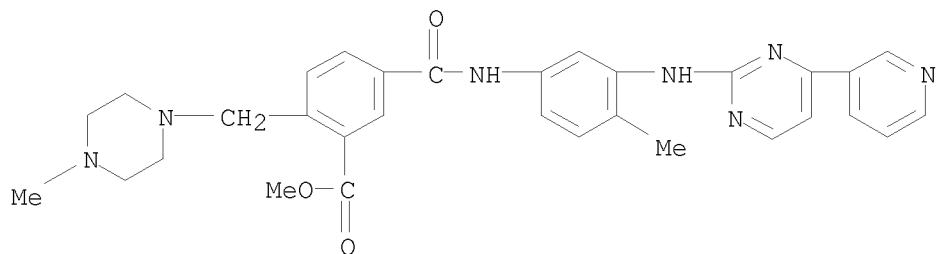
RN 641615-15-8 CAPLUS

CN Benzamide, 3-bromo-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



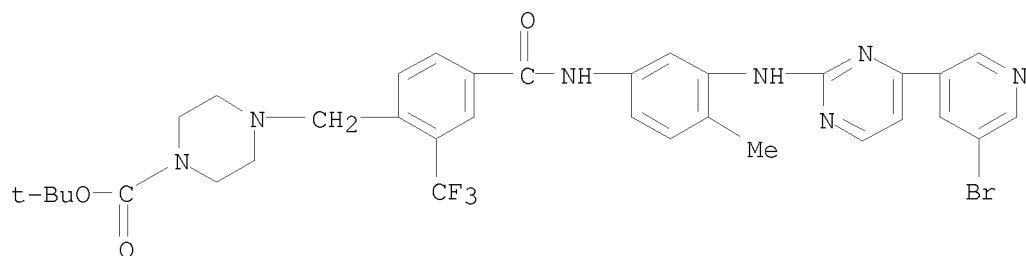
RN 641615-21-6 CAPLUS

CN Benzoic acid, 2-[(4-methyl-1-piperazinyl)methyl]-5-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)



RN 859213-57-3 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[4-[[[3-[[4-(5-bromo-3-pyridinyl)-2-pyrimidinyl]amino]-4-methylphenyl]amino]carbonyl]-2-(trifluoromethyl)phenyl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:1080884 CAPLUS

DN 142:56339

TI Process for the preparation of the anti-cancer drug imatinib and its analogs via aminolysis of a (chloromethyl)benzamide intermediate

IN Kompella, Amala; Bhujanga Rao, Adibhatla Kali Sathya; Venkaiah Chowdary, Nannapaneni; Srinivas, Rachakonda

PA Natco Pharma Limited, India

SO PCT Int. Appl., 65 pp.

CODEN: PIXXD2

not prior

DT Patent

LA English

FAN.CNT 1

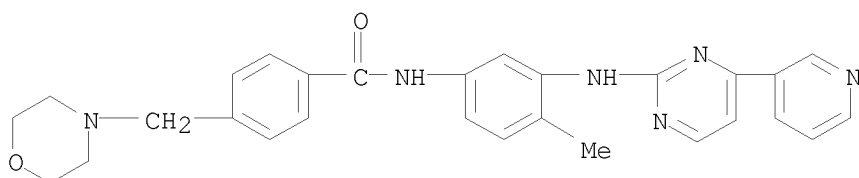
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108699	A1	20041216	WO 2003-IN211	20030606
W: AE, AG, AL, AM, AN, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242988	A1	20050104	AU 2003-242988	20030606
PRAI WO 2003-IN211	A	20030606		

OS CASREACT 142:56339

AB The invention discloses a process for the manufacture of imatinib [I; X = 4-methylpiperazin-1-yl] and three of its new analogs I [X = morpholin-4-yl, piperidin-1-yl, and imidazol-1-yl] through aminolysis of the intermediate I [X = Cl]. The mesylate (methanesulfonate) salt of imatinib is a popular life-saving drug, used to treat chronic myelogenous leukemia (CML). The other compds. are claimed as protein tyrosine kinase inhibitors (no data). The new process involves fewer steps (7) than the 9 steps in the known process disclosed in EP 0564409 and US 55211584, making the new process simple and cost effective. Yields are fairly high in all steps (65-90%), as compared to 20-50% realized by the prior art process. Reaction times are fairly low (8-10 h) in all steps, as compared to the time (12-25 h) for most of the stages in the prior art process. Obnoxious, foul smelling, and difficult-to-handle reagents are avoided, making the process safe and environmentally safe for com. application. Column chromatog., which is not practical on com. scale, is avoided at all stages. Consequently the process is simple and economical. Thus, 2-amino-4-nitrotoluene in BuOH was treated with HNO<sub>3</sub> and then with aqueous cyanamide, and the mixture was heated at 90-95° for 12 h, to give 61% yield of 2-methyl-5-nitrophenylguanidine nitrate (II) on a 22-kg scale, with simple recovery of pure, unreacted 2-amino-4-nitrotoluene from the mother liquors, also on a multi-kg scale. Cyclization of II with 3-(dimethylamino)-1-(3-pyridyl)-2-propen-1-one in refluxing BuOH in the presence of NaOH for 10 h gave intermediate III quant., with III being isolated in 88% yield on a 21-kg scale. This was followed by reduction of the nitro group of III, using SnCl<sub>2</sub> in concentrated HCl, to give the corresponding amine in 61.5% yield, on a 10-kg scale. The amine was amidated with 4-(ClCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>COCl (preparation given) using Et<sub>3</sub>N in CHCl<sub>3</sub>, giving the (chloromethyl)benzamide intermediate I [X = Cl] in 70% yield on a 13.9-kg

scale. This compound reacted with N-methylpiperazine in DMF over 4 h at 20-40°, giving imatinib free base after extraction into CHCl<sub>3</sub>, carbon treatment, evaporation, and trituration with EtOAc. Imatinib was obtained in 61% yield, 99.8% purity by HPLC, and on a 9.8-kg scale. The other three products I were obtained almost identically, using different amines in the final step.

IT 404843-98-7P, 4-(Morpholinomethyl)-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide  
 RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (target compound; manufacture of imatinib and analogs via aminolysis of (chloromethyl)benzamide intermediate)  
 RN 404843-98-7 CAPLUS  
 CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:1060780 CAPLUS

DN 142:38275

TI Preparation of N-phenyl-2-pyrimidine-amine derivatives as anticancer agents and process for the preparation thereof

IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jin; Lee, Gong-Yeal; Kim, Hong-Youb; Woo, Seok-Hun; Kim, Yong-Seok; Bae, Woo-Chul; Lee, Sun-Ahe; Han, Byoung-Cheol

PA Il Yang Pharm. Co., Ltd., S. Korea

SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 446,446, abandoned.

CODEN: USXXCO

DT Patent

not prior

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004248918	A1	20041209	US 2004-806834	20040322
PRAI	KR 2003-28669	A	20030506		
	US 2003-446446	B2	20030528		

OS MARPAT 142:38275

AB The title compds. (I) [R1 = 3- or 4-pyridyl; R2, R3 = H, lower alkyl; R6, R7 = Q; wherein X = O, NH; n = 0, 1; R9 = C5-10 9 aliphatic radical, 5- to 7-membered (un)saturated monocyclic radical, or bi- or tricyclic radical optionally combined with benzene ring, each of which has 1 to 3 hetero atoms selected from a group consisting of N, O, and S, piperazinyl or homopiperazinyl each of which is substituted by lower alkyl; R4, R5, R7, R8 = H or one or two thereof each represent halogen, lower alkyl, or lower alkoxy; when R6 is Q, or one or two of R4, R5, R6, and R8 each represent halogen, lower alkyl, or lower alkoxy; when R7 is Q, provided that R6 or R7 represents Q wherein n = 0 and R9 = 4-methylpiperazine, then one or more of R4, R5, R7, and R8, or one or more of R4, R5, R6, and R8 are halogen] or salts thereof are prepared These compds. show a superior effect on lung cancer, gastric cancer, colon cancer, pancreatic cancer, hepatoma, prostatic cancer, breast cancer, chronic or acute leukemia, hematol. malignancy, encephalophyma, bladder cancer, rectal cancer, or cervical cancer of warm-blooded animals. The present invention also relates to a process for preparing the compound I, and to a pharmaceutical composition for

the

treatment of the above various diseases, which comprises an effective amount of the compound as an active ingredient together with pharmaceutically acceptable inert carriers. Thus, 3-dimethylamino-1-(3-pyridyl)-2-propen-1-one was cyclocondensed with 2-methyl-5-nitrophenylguanidine nitrate in the presence of sodium hydroxide in isopropanol under reflux for 18 h to give N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine which was reduced by stannous chloride dihydrate in EtOAc/ethanol under reflux for 4 h to give N-(5-amino-2-methylphenyl)-4-(3-pyridyl)-2-pyrimidineamine (II). II underwent amidation with 4-chloromethylbenzoyl chloride in Et3N in THF under reflux for 4 h to give N-[5-(4-chloromethylbenzoylamino)-2-methylphenyl]-4-(3-pyridyl)-2-pyrimidineamine which was stirred with pyridine for 30 min and then refluxed with N-methylhomopiperazine for 12 h to give 4-(4-methylhomopiperazin-1-ylmethyl)-N-[4-methyl-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide (III). III methanesulfonate and 4-[(4-methylpiperazin-1-ylamino)methyl]-N-[4-methyl-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide methanesulfonate showed IC50 of 1.20 and <0.10 µg/mL, resp., against the growth of K562 cells.

IT 796738-40-4P, 4-(4-Methylhomopiperazin-1-ylmethyl)-N-[4-methoxy-3-

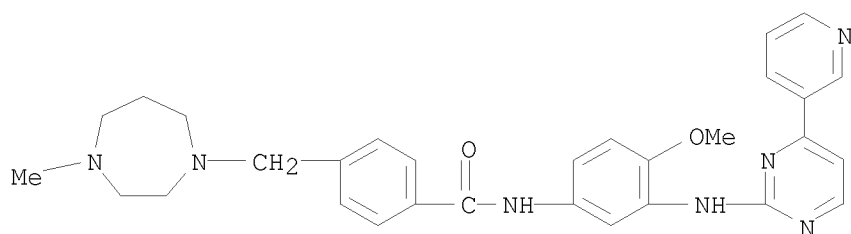
[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-phenylpyrimidine-2-amine derivs. as anticancer agents)

RN 796738-40-4 CAPLUS

CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L22 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:996162 CAPLUS  
 DN 141:424205  
 TI New N-phenyl-2-pyrimidine-amine derivatives related to imatinib mesylate,  
 useful as antitumor agents, and process for their preparation  
 IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jin; Lee, Gong-Yeal; Kim,  
 Hong-Youb; Woo, Seok-Hun; Kim, Yong-Seok; Bae, Woo-chul; Lee, Sun-Ahe;  
 Han, Byoung-Cheol  
 PA Il Yang Pharm. Co. Ltd., S. Korea  
 SO PCT Int. Appl., 55 pp. not prior  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099187	A1	20041118	WO 2004-KR611	20040319
W: AE, AG, AL, AM, AN, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004095155	A	20041112	KR 2004-17594	20040316
PRAI KR 2003-28669	A	20030506		

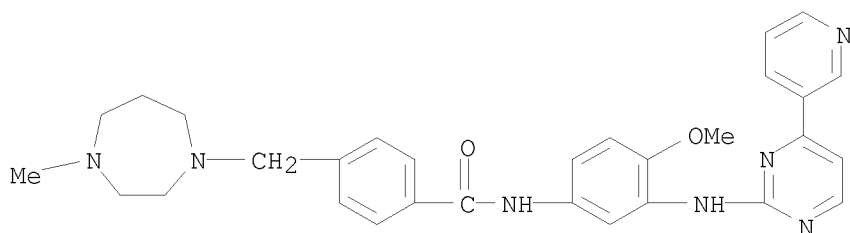
OS MARPAT 141:424205

AB The invention relates to N-phenyl-2-pyrimidine-amine derivs. and their salts, which show superior action against lung cancer, gastric cancer, colon cancer, pancreatic cancer, hepatoma, prostatic cancer, breast cancer, chronic or acute leukemia, hematol. malignancy, encephalophyma, bladder cancer, rectal cancer, or cervical cancer, etc., in warm-blooded animals. The invention also relates to a process for preparing the compds., and to pharmaceutical compns. for the treatment of cancer, etc., which comprise the compds. as active ingredients, together with pharmaceutically acceptable inert carriers. Specifically claimed are compds. I and salts [wherein: R1 = 3-pyridyl or 4-pyridyl; R2, R3 = (independently) H or lower alkyl; R6 or R7 = -NHCO-p-C6H4-CH2XnR9; X = O or NH; n = 0-1; R9 = C5-10 aliphatic, or 5- to 7-membered (un)saturated monocycle, or a bi- or tricyclic radical optionally combined with a benzene ring, each with 1-3 N/O/S heteroatoms, or (homo)piperazinyl substituted by lower alkyl; 1-2 of R4, R5, R6/R7, and R8 = halo, lower alkyl, or lower alkoxy; others = H; provided that when R6 or R7 = said radical and n = 0 and R9 = 4-methylpiperazinyl, then one or more of R4, R5, R6/R7, and R8 is halo]. For example, 3-acetylpyridine was converted in 3 steps to N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine. This nitro compound was reduced to the amine with SnCl2, and the amine was amidated with 4-(ClCH2)C6H4COCl. The obtained 4-(chloromethyl)benzamide derivative was coupled with 1-amino-4-methylpiperazine to give invention compound II, which was converted to the methanesulfonate salt (III). The latter was more than 5-fold more potent than imatinib mesylate against the human CML cell line K562, and was at least as active against other cell lines. Other compds. I showed different spectra of superiority to imatinib mesylate



against the various cancer cell lines. Compound IV (mesylate) had excellent, dose-related therapeutic activity against sarcoma-180 in ICR mice, giving an inhibition ratio of 63.0% at 50 mg/kg i.v. In an oral pharmacokinetic assay in rats, III roughly matched the performance of imatinib mesylate (Tmax, Cmax, and AUC) at half the dosage. III also showed no acute toxicity toward mice at a dose of 2000 mg/kg orally. IV mesylate had an i.v. LD50 of 75-100 mg/kg in mice, still much safer than cisplatin (11 mg/kg i.v.). Although several compds. I are preferred with respect to protein kinase inhibition (no data), II is particularly preferred. Therefore III and IV mesylate are expected to be new and potent therapeutic agents for the treatment of the aforementioned cancers, in addition to CML.

IT 796738-40-4P, 4-[(4-Methylhomopiperazin-1-yl)methyl]-N-[4-methoxy-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (drug candidate; preparation of phenylpyrimidinamine derivs. related to imatinib mesylate as antitumor agents)  
 RN 796738-40-4 CAPLUS  
 CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:996161 CAPLUS  
 DN 141:424204  
 TI New N-phenyl-2-pyrimidine-amine derivatives related to imatinib mesylate,  
 useful as antitumor agents, and process for the preparation thereof  
 IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jn; Lee, Gong-Yeal; Kim, Hong-Youb;  
 Woo, Seok-Hun; Bae, Woo-chul; Lee, Sun-Ahe; Han, Byoung-Ceol  
 PA Il Yang Pharm Co., Ltd., S. Korea  
 SO PCT Int. Appl., 55 pp.  
 CODEN: PIXXD2  
 DT Patent not prior  
 LA English  
 FAN.CNT 3

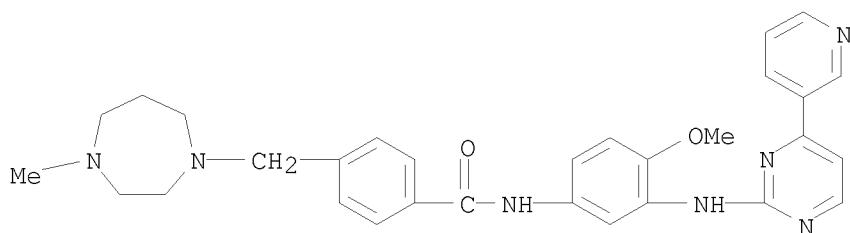
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004099186	A1	20041118	WO 2003-KR1029	20030526
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003232650	A1	20041126	AU 2003-232650	20030526
	KR 2004095155	A	20041112	KR 2004-17594	20040316
PRAI	KR 2003-28669	A	20030506		
	WO 2003-KR1029	W	20030526		

OS MARPAT 141:424204

AB The invention relates to N-phenyl-2-pyrimidine-amine derivs. and their salts, which show superior action against tumors, lung cancer, gastric cancer, etc., in warm-blooded animals. The invention also relates to a process for preparing the compds., and to pharmaceutical compns. for the prevention and treatment of cancer, etc., which comprise the compds. as active ingredients. Specifically claimed are compds. I and salts [wherein: R1 = 3-pyridyl or 4-pyridyl; R2, R3 = (independently) H or lower alkyl; R6 or R7 = -NHCO-p-C6H4-CH2XnR9; X = O or NH; n = 0-1; R9 = C5+ aliphatic or heterocycle, or (homo)piperazinyl substituted by lower alkyl; 1-2 of R4, R5, R6/R7, and R8 = halo, lower alkyl, or lower alkoxy; others = H; provided that when R6 or R7 = said radical and n = 0 and R9 = 4-methylpiperazinyl, then one or more of R4, R5, R6/R7, and R8 is halo]. For example, 3-acetylpyridine was converted in 3 steps to N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine. This nitro compound was reduced to the amine with SnCl2, and the amine was amidated with 4-(ClCH2)C6H4COCl. The obtained 4-(chloromethyl)benzamide derivative was coupled with 1-amino-4-methylpiperazine to give invention compound II, which was converted to the methanesulfonate salt (III). The latter was more than 5-fold more potent than imatinib mesylate against the human CML cell line K562, and was at least as active against other cell lines. Other compds. I showed different spectra of superiority to imatinib mesylate against the various cancer cell lines. In an oral pharmacokinetic assay in rats, III roughly matched the performance of imatinib mesylate (Tmax, Cmax, and AUC) at half the dosage. III also showed no acute toxicity toward mice at a dose of 2000 mg/kg orally. Although several compds. I are preferred with respect to protein kinase inhibition (no data), II is

particularly preferred.

IT 796738-40-4P, 4-[(4-Methylhomopiperazin-1-yl)methyl]-N-[4-methoxy-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (drug candidate; preparation of phenylpyrimidinamine derivs. related to imatinib mesylate as antitumor agents)  
 RN 796738-40-4 CAPLUS  
 CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:589375 CAPLUS  
 DN 141:140459  
 TI Preparation of sulfamides as anti-cancer agents  
 IN Flynn, Daniel L.; Petrillo, Peter A.  
 PA Deciphera Pharmaceuticals, Inc., USA  
 SO PCT Int. Appl., 168 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 5

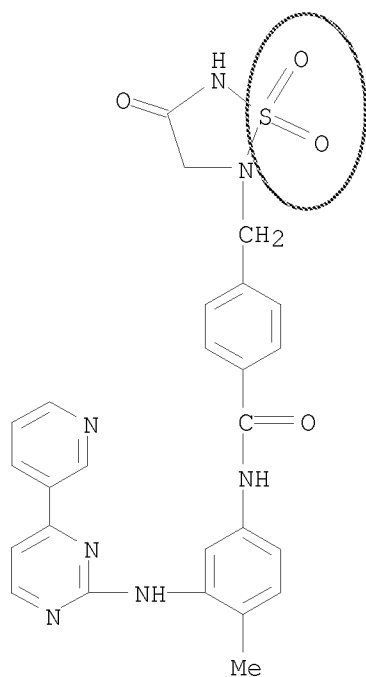
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060305	A2	20040722	WO 2003-US41425	20031226
	WO 2004060305	A3	20050210		
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	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				
	PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,				
	UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				
	BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				
	ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,				
	TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004171075	A1	20040902	US 2003-746545	20031224
	US 2004176395	A1	20040909	US 2003-746607	20031224
	US 7279576	B2	20071009		
	CA 2511840	A1	20040722	CA 2003-2511840	20031226
	AU 2003303639	A1	20040729	AU 2003-303639	20031226
	EP 1590344	A2	20051102	EP 2003-814980	20031226
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003017863	A	20051206	BR 2003-17863	20031226
	CN 1756849	A	20060405	CN 2003-80110049	20031226
	CN 1791596	A	20060621	CN 2003-80110048	20031226
	JP 2006519765	T	20060831	JP 2005-508623	20031226
	IN 2005CN01433	A	20070302	IN 2005-CN1433	20050628
PRAI	US 2002-437304P	P	20021231		
	US 2002-437403P	P	20021231		
	US 2002-437415P	P	20021231		
	US 2002-437487P	P	20021231		
	US 2003-463804P	P	20030418		
	US 2003-746545	A	20031224		
	US 2003-746607	A	20031224		
	WO 2003-US41425	W	20031226		
OS	MARPAT 141:140459				
AB	Sulfamides, such as I, were prepared for use as anticancer agents which act by modulating the activation states of abl or bcr-abl $\alpha$ -kinase proteins. Thus, 4-HO2CC6H4CH2NHSO2NHCOR [R = pyrrolidino], prepared from 4-MeO2CC6H4CH2NH2 and pyrrolidine, was treated with the pyrimidinylaminoaniline fragment to give I, which showed 10% inhibition of non-phosphorylated abl kinase at 10 $\mu$ M.				
IT	726192-44-5P 726192-54-7P 726192-56-9P 726192-57-0P				
	RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES				

(Uses)

(preparation of sulfamides as anti-cancer agents)

RN 726192-44-5 CAPLUS

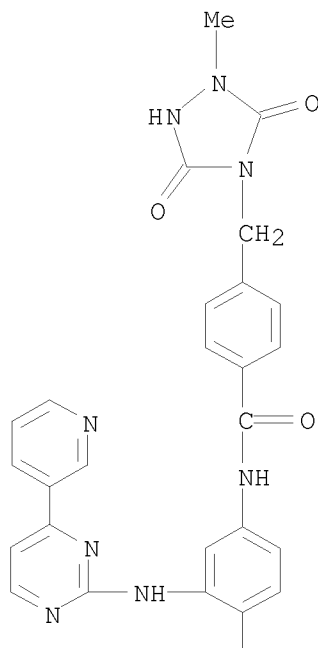
CN Benzamide, 4-[(1,1-dioxido-4-oxo-1,2,5-thiadiazolidin-2-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 726192-54-7 CAPLUS

CN Benzamide, 4-[(1-methyl-3,5-dioxo-1,2,4-triazolidin-4-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

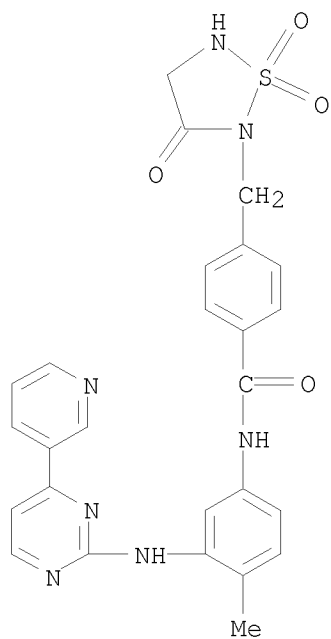
PAGE 1-A



PAGE 2-A



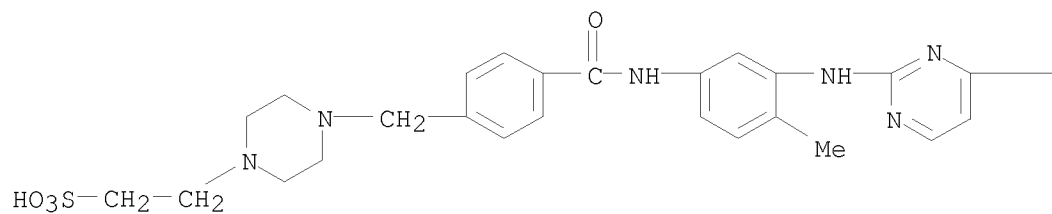
RN 726192-56-9 CAPLUS  
 CN Benzamide, 4-[(1,1-dioxido-3-oxo-1,2,5-thiadiazolidin-2-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



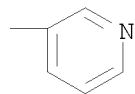
RN 726192-57-0 CAPLUS

CN 1-Piperazineethanesulfonic acid, 4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L22 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:20664 CAPLUS  
 DN 140:77165  
 TI Preparation of 4-[(4-methylpiperazin-1-yl)methyl]benzamide for treatment  
 of leukemia  
 IN Asaki, Tetsuo; Hamamoto, Taisuke; Sugiyama, Yukiteru  
 PA Nippon Shinyaku Co., Ltd., Japan  
 SO PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002963	A1	20040108	WO 2003-JP8192	20030627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2490907	A1	20040108	CA 2003-2490907	20030627
AU 2003246100	A1	20040119	AU 2003-246100	20030627
BR 2003012288	A	20050412	BR 2003-12288	20030627
EP 1533304	A1	20050525	EP 2003-738555	20030627
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CN 1678590	A	20051005	CN 2003-820146	20030627
MX 2004PA12845	A	20050224	MX 2004-PA12845	20041216
US 2006014742	A1	20060119	US 2004-519722	20041228
PRAI JP 2002-189269	A	20020628		
JP 2002-305146	A	20021018		
JP 2002-377937	A	20021226		
WO 2003-JP8192	W	20030627		

OS MARPAT 140:77165

AB The title compds. I [wherein R1 = saturate cyclic amino, alkylamino, or dialkylamino; R2 = alkyl, halo, haloalkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxy carbonyl, acyl, amino, alkylamino, dialkylamino, NO2, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, or CN; R3 = H, halo, or alkoxy; Het1 = pyridyl, Ph, pyrimidyl, pyrazinyl, or triazinyl; Het2 = pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, or 1,2-dihydropyridazinyl; etc.] or salts thereof are prepared as BCR-ABL tyrosine kinase inhibitors, and are useful for the treatment of leukemia (no data). For example, the compound II was prepared in a multi-step synthesis. II showed inhibitory activities with IC50 of 0.0008 and 3.99  $\mu$ M against cell proliferation of K562 and U937, resp., in cow. Formulations containing I as an active ingredient were also described.

IT 641615-04-5P 641615-05-6P 641615-07-8P

641615-08-9P 641615-15-8P 641615-21-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

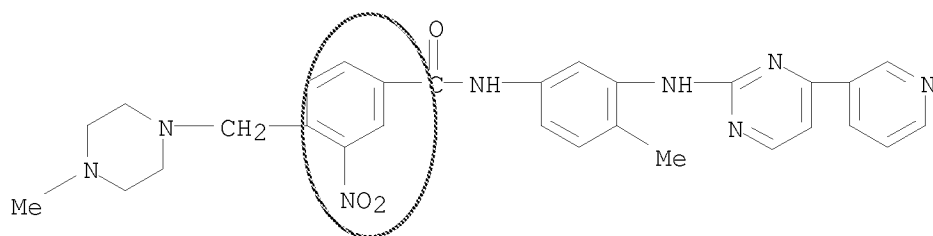
(drug candidate; preparation of [(piperazinyl)methyl]benzamides for



treatment of leukemia)

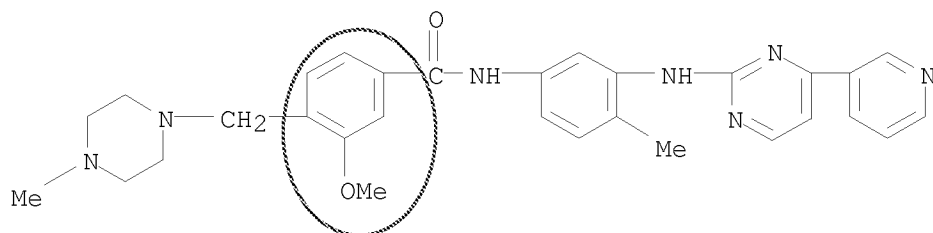
RN 641615-04-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-3-nitro- (CA INDEX NAME)



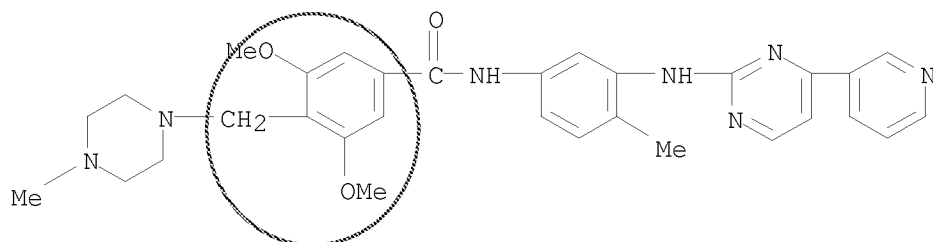
RN 641615-05-6 CAPLUS

CN Benzamide, 3-methoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



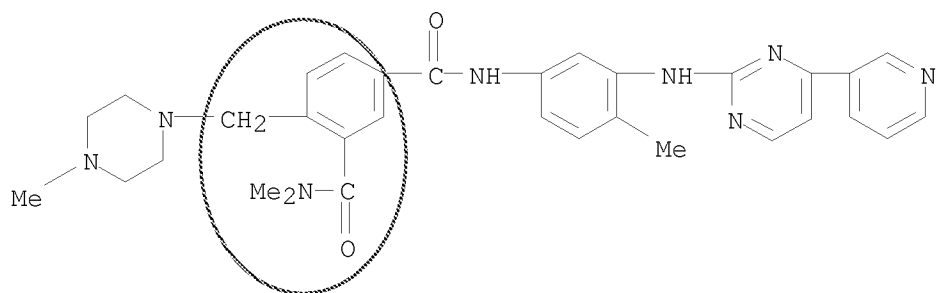
RN 641615-07-8 CAPLUS

CN Benzamide, 3,5-dimethoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



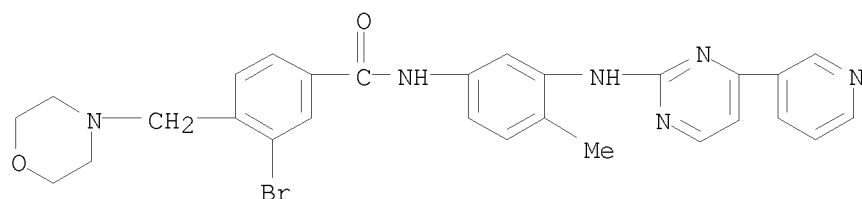
RN 641615-08-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N3,N3-dimethyl-4-[(4-methyl-1-piperazinyl)methyl]-N1-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 641615-15-8 CAPLUS

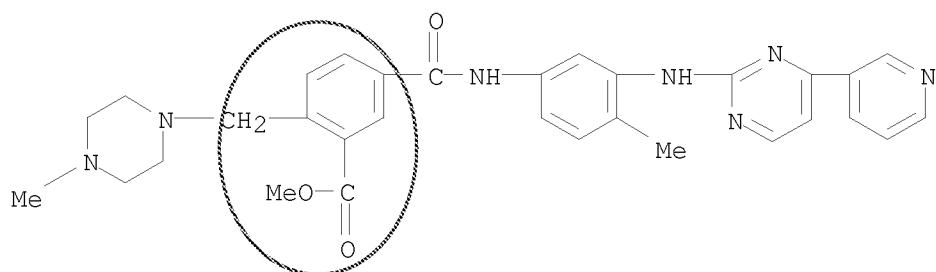
CN Benzamide, 3-bromo-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



no N-oxide or oxo substituent on A

RN 641615-21-6 CAPLUS

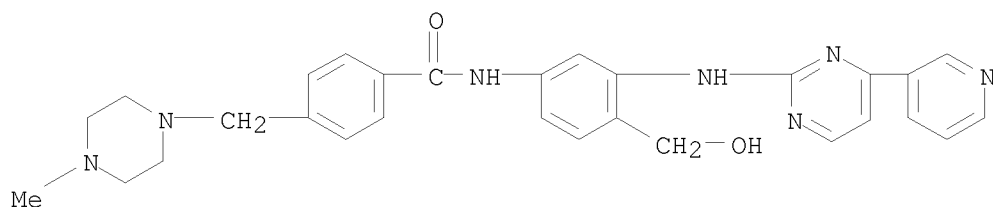
CN Benzoic acid, 2-[(4-methyl-1-piperazinyl)methyl]-5-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2003:591164 CAPLUS  
 DN 139:149642  
 TI Preparation of benzoylaminophenylaminopyrimidinylpyridines as antitumor agents  
 IN Boernsen, Klaus Olaf; End, Peter; Gross, Gerhard; Pfaar, Ulrike  
 PA Novartis Ag, Switz.; Novartis Pharma GmbH  
 SO PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

Appl. WIPO

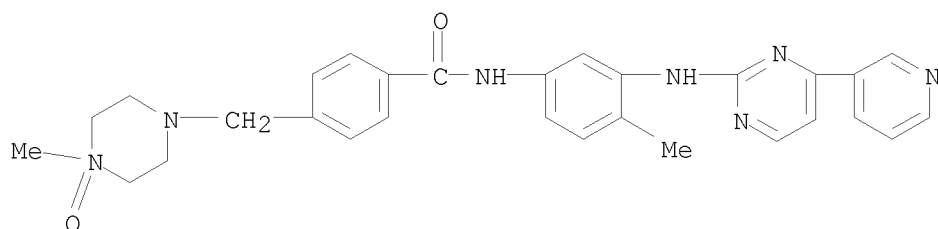
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003062220	A1	20030731	WO 2003-EP613	20030122
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
	CA 2474104	A1	20030731	CA 2003-2474104	20030122
	EP 1470120	A1	20041027	EP 2003-731700	20030122
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003007058	A	20041228	BR 2003-7058	20030122
	JP 2005519908	T	20050707	JP 2003-562099	20030122
	CN 1646519	A	20050727	CN 2003-802708	20030122
	EP 1783126	A2	20070509	EP 2007-101787	20030122
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, SE, SI, SK, TR, RO				
	IN 2004CN01599	A	20060224	IN 2004-CN1599	20040720
	MX 2004PA07130	A	20041029	MX 2004-PA7130	20040723
	US 2005209452	A1	20050922	US 2005-502291	20050429
PRAI	GB 2002-1508	A	20020123		
	EP 2003-731700	A3	20030122		
	WO 2003-EP613	W	20030122		
OS	MARPAT 139:149642				
AB	Title compds. I [R1 = , OH; R2 = H, alkyl, hydroxyalkyl; A = NR3R4, CR3R4, OR3R4; R3R4 = (un)substituted alkylene, oxaalkylene, azaalkylene; at least one N atom is substituted by O] were prepared for use as antitumor agents (no data). Thus, I [R1 = H, R2 = Me, A = 4-methyl-4-oxido-1-piperazinyl] was prepared by oxidation of I [R1 = H, R2 = Me, A = 4-methyl-1-piperazinyl].				
IT	571186-90-8P 571186-91-9P 571186-92-0P 571186-93-1P 571186-94-2P 571186-95-3P RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of benzoylaminophenylaminopyrimidinylpyridines as antitumor agents)				
RN	571186-90-8 CAPLUS				
CN	Benzamide, N-[4-(hydroxymethyl)-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)				



claim 33

RN 571186-91-9 CAPLUS

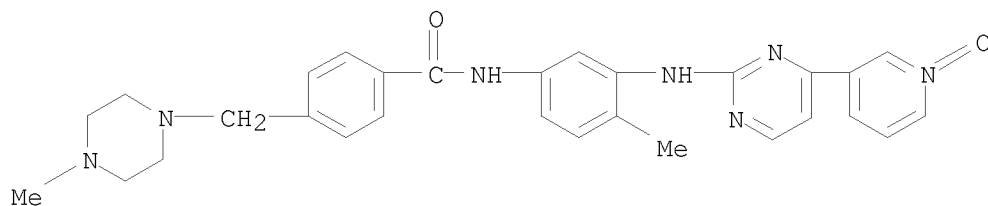
CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



claim 30

RN 571186-92-0 CAPLUS

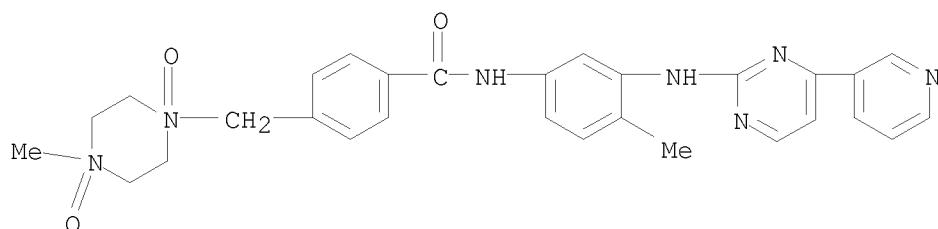
CN Benzamide, N-[4-methyl-3-[[4-(1-oxido-3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



claim 31

RN 571186-93-1 CAPLUS

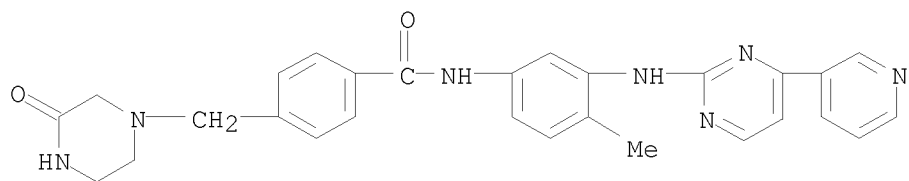
CN Benzamide, 4-[(4-methyl-1,4-dioxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



claim 32

RN 571186-94-2 CAPLUS

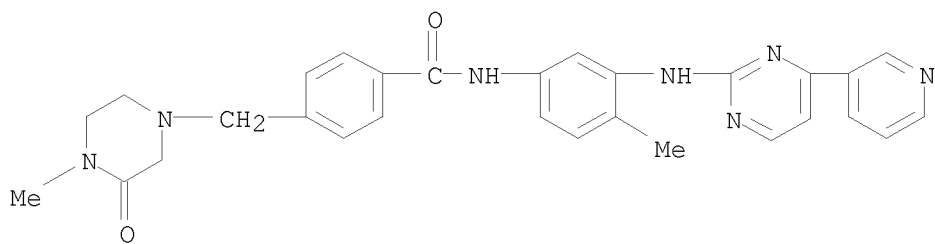
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(3-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



Claim 25

RN 571186-95-3 CAPLUS

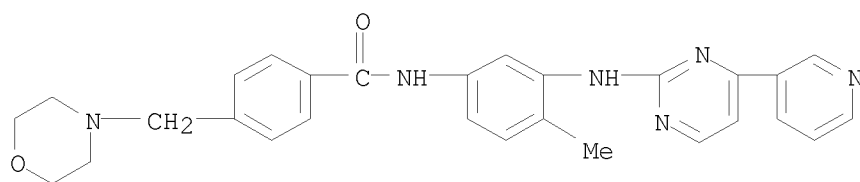
CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



claim 26

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2003:409452 CAPLUS  
 DN 139:226295  
 TI Two distinct phosphorylation pathways have additive effects on Abl family kinase activation  
 AU Tanis, Keith Q.; Veach, Darren; Duewel, Henry S.; Bornmann, William G.; Koleske, Anthony J.  
 CS Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT, 06520, USA  
 SO Molecular and Cellular Biology (2003), 23(11), 3884-3896  
 CODEN: MCEBD4; ISSN: 0270-7306  
 PB American Society for Microbiology  
 DT Journal  
 LA English  
 AB The activities of the related Abl and Arg nonreceptor tyrosine kinases are kept under tight control in cells, but exposure to several different stimuli results in a two- to fivefold stimulation of kinase activity. Following the breakdown of inhibitory intramol. interactions, Abl activation requires phosphorylation on several tyrosine residues, including a tyrosine in its activation loop. These activating phosphorylations have been proposed to occur either through autophosphorylation by Abl in trans or through phosphorylation of Abl by the Src nonreceptor tyrosine kinase. The authors show here that these two pathways mediate phosphorylation at distinct sites in Abl and Arg and have additive effects on Abl and Arg kinase activation. Abl and Arg autophosphorylate at several sites outside the activation loop, leading to 5.2- and 6.2-fold increases in kinase activity, resp. The authors also find that the Src family kinase Hck phosphorylates the Abl and Arg activation loops, leading to an addnl. twofold stimulation of kinase activity. The autoactivation pathway may allow Abl family kinases to integrate or amplify cues relayed by Src family kinases from cell surface receptors.  
 IT 404843-98-7, WGB-BC 22  
 RL: BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)  
 (inhibitor; drug sensitivities of Abl and Arg kinases)  
 RN 404843-98-7 CAPLUS  
 CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



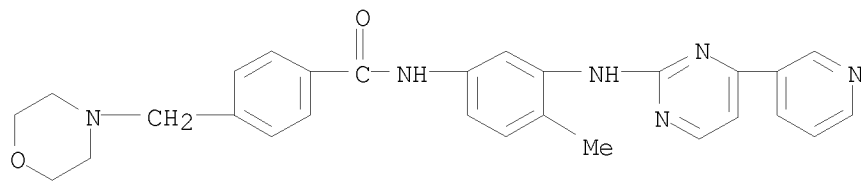
no N-oxide or oxo substituent on A

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2002:220573 CAPLUS  
 DN 136:247605  
 TI N-phenyl-2-pyrimidinamine derivatives as tyrosine kinase inhibitors  
 IN Buerger, Hans Michael; Caravatti, Giorgio; Zimmermann, Juerg; Manley, Paul  
 William; Breitenstein, Werner; Cudd, Margaret Amelia  
 PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft  
 m.b.H.  
 SO PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022597	A1	20020321	WO 2001-EP10503	20010911
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2416274	A1	20020321	CA 2001-2416274	20010911
	AU 200218167	A	20020326	AU 2002-18167	20010911
	BR 2001013838	A	20030603	BR 2001-13838	20010911
	EP 1322634	A1	20030702	EP 2001-984640	20010911
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004509111	T	20040325	JP 2002-526850	20010911
	CN 1525967	A	20040901	CN 2001-815539	20010911
	CN 1872850	A	20061206	CN 2006-10100258	20010911
	US 2004102453	A1	20040527	US 2003-363841	20030310
	US 7081532	B2	20060725		
	US 2006223818	A1	20061005	US 2006-448649	20060607
PRAI	GB 2000-22438	A	20000913		
	CN 2001-815539	A3	20010911		
	WO 2001-EP10503	W	20010911		
	US 2003-363841	A3	20030310		

OS MARPAT 136:247605  
 AB The N-phenyl-2-pyrimidinamines I [R = substituted Ph; R1 = (un)substituted pyrazinyl, 1-methylpyrrolyl, aminophenyl, aminoalkylphenyl, indolyl, imidazolyl, pyridyl, pyridyl N-oxide; R2, R3 = H, alkyl] were prepared for use as tyrosine kinase inhibitors with IC50 of 3-300 nM. Thus, the benzamide II [R4 = 4-ethylpiperazino] was prepared from II [R4 = Cl] and 1-ethylpiperazine.  
 IT 404843-98-7P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of N-phenyl-2-pyrimidinamine derivs. as tyrosine kinase inhibitors)  
 RN 404843-98-7 CAPLUS  
 CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



no N-oxide or oxo substituent on A

RE.CNT 3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/502,291

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

74.25

434.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-10.92

-10.92

STN INTERNATIONAL LOGOFF AT 12:16:40 ON 13 NOV 2007